Modern Concepts of Cardiovascular Disease

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THE CLINICAL SIGNIFICANCE OF PHYSIOLOGICAL STUDIES IN CARDIAC DECOMPENSATION IN MAN

PART II

The volume of the circulating blood is increased in cardiac decompensation with little or no change in the percentage of cells. This differs from mountain sickness, in which the percentage of cells is markedly increased. Deviations from the normal blood volume in congestive failure are therefore probably not due solely to anoxemia. That anoxemia is a factor, however, is suggested by the reticulocytosis seen at the onset of congestive failure and the massive blood destruction with the production of large amounts of bile pigments during recovery. The latter contributes to the jaundice of cardiac decompensation. An additional cause of the increase in blood volume in congestive failure may be widespread capillary and venous dilatation, probably due to anoxemia. This increased prominence of thin-walled blood vessels is an important contributory cause in the genesis of cyanosis. The large blood volume itself probably increases pulmonary congestion and is therefore a cause of dyspnea; it may also contribute to venous engorgement.

Lymphatic drainage is important in the removal of accumulations of tissue fluid. This function breaks down in congestive failure, probably as a result of anoxemia, although increased lymphatic pressures consequent to elevated venous pressures also must be important.

Small elevations in rectal temperature are common in severe congestive failure, but the skin temperature is normal or low. This is due to impairment of peripheral blood flow which results in diminished heat dispersal via the skin. A corresponding increase in the heat dispersed via the lungs must occur and is effected by increased respiratory activity. The latter is a cause of dyspnea.

The basal metabolic rate is usually elevated in congestive failure. This is due both to the above-mentioned rise in body temperature and to increased respiratory activity. Levels above +40 per cent are not common except in patients with severe dyspnea; in such instances the readings clearly are invalid since such patients cannot be considered basal.

Hepatic enlargement occurs early in the course of cardiac decompensation. In the absence of pulmonary infarction jaundice appears only as a result of severe cardiac failure; some elevation of serum bilirubin level is present with lesser degrees of decompensation. In animals anoxemia causes hepatic enlargement, central necrosis, and impaired excretion of bilirubin, all of which occur in congestive failure in man. An additional factor giving rise to jaundice during recovery from congestive failure in man is the above-described blood destruction. The changes in the hepatic function in cardiac decompensation are usually not clinically important. They are significant, however, in that they indicate the presence of liver damage which may lead to cirrhosis. In occasional instances upper abdominal pain and vomiting associated with sudden hepatic engorgement may be a presenting symptom.

Evidences of impaired renal physiology are common in cardiac decompensation. Albuminuria and the presence of erythrocytes, leukocytes, and casts in the urine are the rule. The phenolsulphonephthalein excretion is diminished. These findings do not necessarily indicate the presence of nephritis since they can be produced in animals simply by inducing stasis in the kidney. In uncomplicated cardiac decompensation the urinary specific gravity is very high and the urea clearance does not deviate from normal to any significant degree. The rise in blood non-protein nitrogen levels frequently found in patients with severe decompensation is therefore not due solely to impaired renal function; oliguria due to pre-renal deviation of fluids available for urine formation is a major cause of such increases. Accordingly blood non-protein nitrogen concentrations as high as 80 mgm. per cent should not be considered contraindications in themselves to the use of mercurial diuretics. Indeed, satisfactory diuresis induced by the injection of mercurial diuretics usually causes a previously elevated non-protein nitrogen level to return to or toward normal.

Gastrointestinal complaints, including anorexia, nausea, distension, and belching are frequently seen in congestive failure and vomiting is not uncommon. Anoxemia comparable in degree to that seen in cardiac decompensation has been shown to cause decreased tonus and prolonged emptying time of the stomach with diminution in contractions; secretion is not, however, impaired. Abnormal gastrointestinal function may be responsible, at least in part, for the loss of weight, vitamin deficiencies, and decreased plasma protein levels found in chronic cardiac failure. The last named favors the development of edema by lowering the osmotic pressure of the plasma and loss of flesh decreases tissue tension, thereby favoring accumulation of edema and retarding its resorption.

The skeletal muscle shows evidence of abnormal function in congestive failure. Weakness is prominent and creatinuria, possibly due to anoxemia, has been demonstrated; the latter disappears with improvement in congestive failure. The *central nervous system* also functions abnormally as evidenced by coma, psychic disturbances, and Cheyne-Stokes' respiration. Changes in reflexes do not, however, occur.

It is clear from the above discussion that chronic cardiac decompensation causes abnormal function of every organ in the body with the possible exception of the glands of internal secretion. The physiological changes which give rise to the clinical manifestations of congestive failure are obviously very complexly interrelated. That other physiological changes, as yet unrecognized, may occur is likely. It is not the purpose of the present discussion to define precisely the mechanisms underlying all the clinical manifestations of congestive failure, since this has been done in tentative form elsewhere. It is, however, worth-while listing the factors implicated in the genesis of some of them. Thus edema formation is conditioned by capillary dilatation and anoxemia, low plasma protein level, elevated venous pressure, depressed lymphatic function, diminished tissue pressure, and water and sodium chloride intake. Cyanosis is influenced by decreased arterial blood oxygen saturation, increased de-oxygenation

of capillary blood, and capillary and venous dilatation. Dyspnea results from anoxemia due to impaired pulmonary function and abnormal lactic acid metabolism, increased intrapleural pressure, abnormal stimuli from the lungs, increased blood volume, and impaired peripheral heat dispersal.

The widespread physiological changes in congestive failure are all probably secondary to a cardiac output which is low in relation to the metabolic needs of the body and to the venous pressure. Some of these secondary changes may however overshadow lowering of the cardiac output as the direct cause of one symptom or another in some patients. Thus in some instances intrapulmonary changes may be more important in the genesis of dyspnea, or lowering of the plasma protein more important in the genesis of edema than anoxemia due to an inadequate cardiac output. The low cardiac output of congestive failure may, therefore, give rise to the signs and symptoms of cardiac decompensation in many different ways. One mechanism or another may predominate in a given patient, or several may be equally important. A valid generalization concerning the origin of the signs and symptoms of chronic congestive failure is that they are due to a summation of the effect of sub-maximal or even minimal changes in a multiplicity of complexly interrelated factors and that the degree of change in each of these factors, and consequently their importance, varies from patient to patient.

Treatment may be considered under seven main heads.

1. **Digitalis.** Studies on the effect of digitalis on the cardiac output may be summarized as follows: Digitalis causes an increase in the cardiac output of almost all patients with congestive failure and rapid auricular fibrillation, and in some patients with congestive failure and no arrhythmia. The effectiveness of digitalis seems to diminish during successive bouts of cardiac decompensation, apparently more rapidly in patients with regular rhythm than in those with auricular fibrillation. In most of the cases in which the cardiac output increases as a result of digitalization, a complete return to normal values is not secured; in some instances the increase obtained is probably not the most important factor in causing clinical improvement. When clinical improvement occurs as a result of the administration of digitalis, the rise in cardiac output is appreciable and the arteriovenous oxygen difference becomes more nearly normal; the venous blood oxygen tension increases, implying an increase in tissue oxygen tension. The venous pressure falls and increases in total lung volume occur as improvement becomes apparent following digitalis therapy. The blood volume returns toward normal and evidences of increased blood destruction, *viz.*, increases in bile pigment in stools and urine, become evident.

However, in the majority of instances the measurements obtained after improvement due to digitalization occurs are still abnormal to some degrees. Complete physiological recovery is rare. The results of laboratory experiments on the effects of digitalis support the clinical impression that digitalis, though extremely useful, by itself does not usually completely control congestive failure. Indeed in many instances, the administration of that drug is not the most important of the various therapeutic measures employed.

2. **Diuretics.** No change in the cardiac output occurs following the administration of diuretics. Nevertheless striking improvement in edema, and even in cyanosis and dyspnea may occur. These changes are ascribed to the diminution in blood volume, and secondarily in venous pressure, and to changes in the pulmonary physiology which follow disappearance of congestion. Diuretics do not directly improve the fundamental defect in cardiac disease, the low cardiac output, but do effect improvement by favorably affecting certain other physiological abnormalities which supervene in congestive failure.

3. **Oxygen Therapy.** The cardiac output is not affected by the administration of high concentrations of oxygen but changes in arterial blood oxygen saturation, with a consequent improvement in the tissue oxygen tension, do occur. Simultaneously the abnormally high blood lactic acid level may fall to or toward normal. If diuresis occurs, the venous pressure falls. A lowering of the venous pressure level also occurs as a result of the relief of hyperpnea. Oxygen therapy also does not directly influence the fundamental defect, the low cardiac output, of congestive failure, but rather affords improvement through its action on other physiological abnormalities.

4. **Venesection.** Venesection may cause immediate improvement in cyanosis, dyspnea and orthopnea and later may even be followed by diuresis. This cannot be ascribed to any change in cardiac output, since the latter is temporarily diminished because of the transitory decrease in venous return. However, a decrease in blood volume occurs, with a fall in venous pressure and decrease in congestion of the lungs, sufficient to explain the clinical improvement. The improvement in dyspnea is due not only to lessened reflex dyspnea resulting from decreased pulmonary congestion, but also to decreased anoxemia consequent to an increased lung volume, and improvement of the arterial blood oxygen saturation. Similarly such diuresis as may occur is due not only to the lowered blood volume, which causes a withdrawal of fluid from the tissues, and the lowering of the venous pressure, but also the alleviation of anoxemia.

5. **Rest.** Bed rest not only serves the obvious purpose of cutting down activities to or toward a level which the heart can support, but also is important in that it enables patients who are in a state of continuous oxygen debt to discharge it. Patients who exhibit an elevated blood lactic acid level show significant decreases in blood lactic acid if improvement follows marked limitation of activity.

6. **Limitation of Fluid and Salt.** These clearly do not influence the cardiac output, but act to inhibit the accumulation of extracellular fluid.

7. **Morphia.** Morphia in the doses employed in patients with congestive failure exerts no effect on the cardiovascular dynamics or blood chemistry. It does, however, afford the patient rest and relaxation. As pointed out above, cardiac patients may hyperventilate beyond their needs because of abnormal reflexes from the lungs or increased sensitivity of the respiratory center in the brain. Morphia may interrupt the former and depress the latter.

Conclusions for Therapy. Improvement in physiological and in clinical status following digitalis therapy is associated with a partial return of cardiac output toward normal, whereas the favorable response to other forms of therapy such as diuretics, oxygen, venesection, bed rest, morphia and limitation of fluids and salts is due to correction of some of the secondary effects of a lowered output. In many patients with chronic cardiac decompensation the heart loses its responsiveness to digitalis and therapy consists of the other measures outlined above which cause improvement in signs and symptoms by acting on the secondary effects of impaired cardiac function. However, it must be borne in mind that amelioration of these secondary effects of a lowered cardiac output may result in lessening of anoxemia and thereby cause in some cases increase toward normal of the output of the heart.

As a general conclusion, it should be emphasized that physiologically, as well as clinically, chronic congestive failure is a disorder affecting the function of almost all the organs and tissues of the body. Cardiac decompensation gives rise to a large number of complexly interrelated impaired or perverted physiological mechanisms which result in the signs and symptoms of that syndrome. The fundamental defect is, however, a cardiac output which is low in relation to the metabolic needs of the body and the venous pressure.

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